REMARKS

This Amendment is submitted in reply to the Non-Final Office Action mailed on July 8, 2009. The Office Action provided a three-month shortened statutory period in which to respond, ending on October 8, 2009. Accordingly, this amendment is timely submitted. No fees are believed due with this Amendment. The Director is authorized to charge any fees that may be required, or to credit any overpayment to Deposit Account No. 50-4498 in the name of Nestle Nutrition.

Claims 1-4, 6-14 and 16-28 are currently pending. Claims 6, 12 and 18-22 were previously withdrawn. Claims 5, 15 and 29 were previously canceled. In the Office Action, Claim 27 is objected for reasons of informality; Claims 1-4, 7-14, 16 and 23-26 are rejected under 35 U.S.C. §102; Claims 1-4, 7-11, 13-14, 16-17 and 23-28 are rejected under 35 U.S.C. §103. Applicant does not acquiesce in the correctness of the rejections or objections and reserves the right to present specific arguments regarding any rejected or objected-to claims not specifically addressed. Further, Applicant reserves the right to pursue the full scope of the subject matter of the claims in a subsequent patent application that claims priority to the instant application.

In response Claims 1-3, 9, 17, 23-25 and 27-28 have been amended. These amendments do not add new matter. The amendments are supported in the specification at, for example, page 3, lines 24-27; page 6, lines 29-34. In view of the amendments and/or for the reasons set forth below, Applicant respectfully submits that the rejections should be withdrawn.

In the Office Action, Claim 27 has been objected to for a typographical error. Specifically, the Patent Office states that the comma between "amino" and "acids" should be removed. In response, Applicant has amended Claim 27 to delete the comma. Further, Applicant has also amended the present claims for purposes of informalities to correct the markush group language. Applicant submits that the above-described amendments were made for clarification purposes and not to avoid any prior art.

In the Office Action, Claims 1-4, 7-11, 16 and 23-26 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,387,828 to Abbruzzese, et al. ("*Abbruzzese I*"); Claims 1-4, 7-14, 16 and 23-26 are rejected under 35 U.S.C. §102(a) as being anticipated by U.S. Patent No. 6,387,883 to Abbruzzese, et al. ("*Abbruzzese II*") and under 35 U.S.C. §102(e)

as being anticipated by *Abbruzzese II*. In contrast, Applicant respectfully submits that the cited references are deficient with respect to the present claims.

Independent Claims 1-2 recite, in part, that leucine, in free and/or salt form, is present in an amount of at least about 30% to about 95% by weight based on the weight of total amino acids. Independent Claims 23-24 recite, in part, that leucine, in free and/or salt form, is present in an amount of at least about 30% by weight based on the weight of total amino acids. Independent Claims 3, 17, 25 and 28 recite, in part, leucine, in free and/or salt form, is present in an amount of at least about 30% by weight based on the weight of intact protein. Independent Claims 1-3, 17, 25 and 28 also recite, in part, a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90.

Applicant has found that when dietary intake is limited below the optimal level for physiological or patho-physiological reasons, a dietary supplement must be more effective than normal food intake in order to provide a benefit. This is because in this circumstance, when a dietary supplement is given, normal food intake is likely to be reduced by a calorically equivalent amount. Consequently, a supplement designed to limit cancer cachexia, for example, should stimulate muscle protein synthesis to a greater extent than normal food intake and should not interfere with the response to meal intake. Trials of conventional nutritional supplements in patients with cancer cachexia have failed to show appreciable benefit in terms of weight gain or quality of life. Accordingly, there is a need for effective nutritional approaches capable of treating, preventing or ameliorating the effects of tumor-induced weight loss due to, for example, cancer cachexia and/or anorexia.

Applicant has surprisingly found that a formulation containing free essential amino acids as compared to a formulation containing free essential and non-essential amino acids or intact protein alone is optimal. See specification, Examples 1-2. Applicant has also found that nutritional compositions comprising a mixture of essential amino acids in free form and/or in salt form that has particularly high amounts of leucine had a stimulatory effect on muscle protein synthesis. See specification, Example 3.

In addition, Applicant has surprisingly and unexpectedly found that particularly useful compositions for promotion of muscle protein synthesis or controlling tumor-induced weight

loss, such as cachexia, e.g. cancer cachexia, may be obtained by combining essential amino acids in free form and/or in salt form with intact protein. See specification, Example 2. The effect of such a combination is greater than the effect that can be achieved with either type of combination partner alone. In contrast, Applicant respectfully submits that the cited references fail to disclose or suggest every element of the present claims. Further, Applicant also respectfully submits that the skilled artisan would have no reason to modify the cited references to arrive at the present claims.

Abbruzzese I and *II* both fail to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least about 30% by weight based on the weight of intact protein as required by the present independent claims. *Abbruzzese I* and *II* also fail to disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required by independent Claim 3. The Patent Office admits same. See, Final Office Action dated December 15, 2008, page 5.

In the Non-Final Office Action, the Patent Office performs a calculation based on amounts of branched-chain amino acids in an alleged composition and an amount of leucine in the branched-chain amino acids to imply that there is at least about 23% of leucine in the composition. See, Non-Final Office Action, page 5. However, Applicant respectfully submits that this calculation is misguided.

For example, the portion of *Abbruzzese II* cited by the Patent Office states that "[t]he total amount of branched-chain amino acids ("BCAA") useful in the present invention is about 15-50 g/100 g protein (i.e., percent), preferably about 15-25 g/100 g. Thus, an 8 oz container of the nutritional composition would contain up to about 8 g BCAAs per 16 grams of total protein. The daily delivery of BCAAs is about 5-26 g." See, *Abbruzzese II*, column 9, lines 26-31. However, this calculation does not consider that the compositions of *Abbruzzese I* and *II* require a certain amount of a "source of amino-nitrogen," wherein 15-50% by weight of the amino-nitrogen is branched-chain amino acids. See, e.g., *Abbruzzese II*, column 3, line 58-column 4, line 5; column 4, lines 29-33. Therefore, if the compositions of *Abbruzzese I* and *II* require a lower amount of a source of amino-nitrogen, the compositions of *Abbruzzese I* and *II* will have a lower amount of leucine. Accordingly, the portion of the reference cited by the Patent Office is not

necessarily the amount of branched-chain amino acids in the entire composition, but rather, the amount of branched-chain amino acids in the source of amino-nitrogen.

However, even assuming that this calculation is correct, which Applicant does not believe, the Patent Office's calculation assumes the upper-most range of leucine available in the composition. In other words, in a composition comprising 15-50 g/100 g protein of branched-chain amino acids, the Patent Office's calculation assumes 50 g/100 g protein (i.e., 50%) to arrive at an implied amount of 23% leucine. Even considering the Patent Office's argument regarding the use of "about" to allow for "some tolerance in the ranges," the skilled artisan would understand that a composition having about 23% leucine would be entirely distinguishable from a composition having about 30% leucine, as is required, in part, by the present claims. As is inherently admitted by the use of the greatest amount of branched-chain amino acids, the compositions of *Abbruzzese I* and *II* cannot contain more than about 23% leucine.

Further, the case law cited by the Patent Office is outdated with respect to a recent case decided by the Federal Circuit and regarding interpretation of the word "about." In a 2007 opinion, the Federal Circuit stated that the term "about" must be interpreted in its technological and stylistic context." *Ortho-McNeil Pharmaceutical, Inc. v. Caraco Pharmaceutical Labs, Ltd.*, 476 F.3d 1321, 1326 (Fed. Cir. 2007). To properly interpret the term "about," the Federal Circuit further stated that the use of the term in the patent specification, prosecution history, and claims should aid in determining how the inventor intended the term to be used. *Id.* Taken in its "technological and stylistic context" in this case, the skilled artisan would recognize a composition having about 23% leucine would be entirely distinguishable from a composition having about 30% leucine, as is required, in part, by the present claims.

Applicant also respectfully submits that the skilled artisan would not arrive at the claimed invention using *Abbruzzese I* or *II* in the absence of hindsight because the cited reference fails to recognize the surprising and unexpected benefits of the claimed compositions having optimal amounts of leucine and essential amino acids. Applicant respectfully submits that the Patent Office is using Applicant's patent application as a road map for creating hindsight obviousness and has failed to set forth sufficient reasons for how the skilled artisan would arrive at the claimed invention in view of *Abbruzzese I* and *II*.

Since both *Abbruzzese I* and *II* share the same specification, both of the references are directed to methods and nutritional compositions for preventing and treating cachexia and anorexia. The compositions of *Abbruzzese I* and *II* includes effective amounts of (1) ω3 fatty acids, such as α-linolenic acid, stearidonic acid, eicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid or mixtures thereof; (2) branched-chain amino acids, such as valine, leucine, isoleucine or mixtures thereof; with or without reduced levels of tryptophan and 5-hydroxytryptophan; and (3) an anti-oxidant system selected from the group consisting of beta-carotene, vitamin C, vitamin E, selenium, or mixtures thereof. See, e.g., *Abbruzzese II*, column 3, lines 15-56.

In the only example that utilizes leucine, *Abbruzzese I* and *II* teach an amino acid profile for his nutritional composition with leucine in an amount of 9.08 g/100 g protein (i.e. 9.08%), which is substantially lower than that of the present claims and actually teaches away from same. See, e.g., *Abbruzzese II*, column 9, line 17. Moreover, in the compositions of *Abbruzzese I* and *II*, the ratio of total essential amino acids and conditionally essential amino acids to total amino acids is 0.51, which is also much lower than that of the present claims. As a result, there is no teaching or suggestion to the skilled artisan to optimize the leucine range and amino acid ratios of *Abbruzzese I* or *II* in accordance with that of the present claims in the absence of hindsight.

The Patent Office asserts that finding the optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids would have been obvious to the skilled artisan for the sole reason that *Abbruzzese I* and *II* teach nutritional compositions for treating cancer cachexia. However, this conclusory statement is not sufficient to establish a *prima facie* case of obviousness without some objective reason to utilize the teachings of the references to arrive at the invention. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness by the Patent Office. *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Applicant respectfully submits that there is absolutely no guidance in *Abbruzzese I* or *II* for one of skill in the art to choose the active components and effective amount of the components present in the instant claims to achieve the unexpectedly improved composition as

Applicant has done. To arrive at the claimed optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids in accordance with the present claims, the skilled artisan would have to select these specific components from the teachings of the numerous ω3 fatty acids, branched-chain amino acids, carbohydrates, and anti-oxidant systems taught by *Abbruzzese I* and *I* and then combine them in the specified amounts in a composition. To accomplish this, the skilled artisan would have to perform an undue amount of experimentation to arrive at the specific components and ranges recited by the present claims. The sheer quantity of experimentation necessary to arrive at the composition would be excessive. Moreover, *Abbruzzese I* and *II* do not provide any direction or guidance for using leucine over any other amino acid, and there would be thousands of combinations that would not include any of leucine.

In sum, the skilled artisan would have no reason to arrive at the optimal conditions of the claimed invention using *Abbruzzese I* or *II* in the absence of hindsight. Moreover, *Abbruzzese I* and *II* fail to even recognize the advantages, benefits and/or properties of compositions having leucine and essential amino acids in accordance with the present claims. Instead, Applicant respectfully submits that the Patent Office is improperly using Applicant's patent application as a road map for creating hindsight obviousness.

For at least the above-mentioned reasons, Applicant respectfully submits that *Abbruzzese I* and *II* fail to anticipate the present claims.

Accordingly, Applicant respectfully requests that the anticipation rejections with respect to *Abbruzzese I* and *Abbruzzese II* be reconsidered and withdrawn.

In the Office Action, Claims 1-4, 7-11, 13-14, 16-17 and 23-28 are rejected under 35 U.S.C. §103(a) as being unpatentable over *Abbruzzese I* in view of U.S. Patent No. 6,420,342 to Hageman, et al. ("*Hageman*") and U.S. Patent No. 6,953,679 to Salvati, et al. ("*Salvati*"). Applicant respectfully disagrees with and traverses these rejections for at least the reasons set forth below.

Hageman and *Salvati* fail to remedy the deficiencies of *Abbruzzese I.* For example, *Hageman* and *Salvati* fail to disclose or suggest leucine, in free and/or salt form, is present in an amount of at least about 30% by weight based on the weight of intact protein as required by the present claims. *Hageman* and *Salvati* also fail to disclose or suggest a ratio of total essential

amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required by independent Claims 3, 17, 25 and 28.

Applicant also respectfully submits that the skilled artisan would not arrive at the claimed invention using *Hageman* and *Salvati* in the absence of hindsight because the cited references are entirely directed to compositions utilizing different nutritional ingredients for different intended purposes. Moreover, *Hageman* and *Salvati* fail to even recognize the surprising and unexpected benefits of the claimed compositions having optimal amounts of leucine and essential amino acids. Applicant respectfully submits that the Patent Office is using Applicant's patent application as a road map for creating hindsight obviousness and has failed to set forth sufficient reasons for how the skilled artisan would arrive at the claimed invention in view of *Hageman* and *Salvati*.

Hageman generally describes a nutritional, pharmaceutical or dietetic preparation that includes effective amounts of ribose and folic acid, optionally combined with other components, such as niacin, histidine, glutamine, orotate, vitamin B6 and other components. See *Hageman*, column 5, lines 8-52. *Hageman* also discloses products having the following mixture of amino acids as beneficial for muscle growth when consumed in an amount of more than 2 and preferably more than 4 g per daily dose: 3-10 wt % histidine, 5-15 wt % isoleucine, 10-23 wt % leucine, 10-23 wt % lysine, 515 wt % methionine, 5-15 wt % phenylalanine, 5-15 wt % threonine. See *Hageman*, column 6, line 62-column 7, line 1. The maximum level of leucine of *Hageman's* composition is 23%, which is lower than that of the present claims.

Salvati generally describes fused cyclic compounds and methods of using such compounds in the treatment of nuclear hormone receptor-associated diseases such as cancer and immune disorders and pharmaceutical compositions containing such compounds. See *Salvati*, Abstract. *Salvati*, along with *Hageman*, lists leucine as one of many amino acids and fails to recognize or suggest any superior benefit from increased levels of leucine beyond what is taught. Consequently, the skilled artisan would have no reason to optimize the leucine range of *Hageman* and *Salvati* in accordance with that of the present claims in the absence of hindsight.

The Patent Office asserts that finding the optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids would have

been obvious to the skilled artisan in view of *Hageman* and *Salvati* teachings. However, this conclusory statement is not sufficient to establish a *prima facie* case of obviousness without some objective reason to utilize the teachings of the references to arrive at the invention. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). There must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness by the Patent Office. *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).

Applicant respectfully submits that there is absolutely no guidance in *Hageman* and *Salvati* for one of skill in the art to choose the active components and effective amount of the components present in the instant claims to achieve the unexpectedly improved composition as Applicant has done. To arrive at the claimed optimal ranges of leucine or ratio of total essential amino acids and conditionally essential amino acids to total amino acids in accordance with the present claims, the skilled artisan would have to select these specific components from the numerous components taught by *Hageman* and *Salvati*. *Hageman* teaches the use of ribose, folate, magnesium, niacin, selenium, thiamine, glucose, citrate, histidine, phosphate, sulfate and vitamin B12 and numerous amino acids as active components in his composition. See *Hageman*, columns 5-6. *Salvati* teaches thousands of possible fused cyclic compounds that can be part of his nutritional composition along with whey protein or casin, amino acids, triglycerides, vitamins, minerals, carnitine, lipoic acid, creatine, and coenzyme Q-10. See *Salvati*, columns 3-8.

The skilled artisan would have to perform an undue amount of experimentation based on the thousands of individual compounds listed by *Hageman* and *Salvati* to arrive at the specific components and ranges recited by the present claims. The sheer quantity of experimentation necessary to arrive at the composition would be excessive. Moreover, *Hageman* and *Salvati* do not provide any direction or guidance for using leucine over any other amino acid, and there would be thousands of combinations that would not include any of leucine. As a result, there is no reason that the skilled artisan would optimize the leucine range or amino acid ratios of *Hageman* and *Salvati* in accordance with that of the present claims.

In sum, the skilled artisan would have no reason to arrive at the optimal conditions of the claimed invention using *Hageman* and *Salvati* in the absence of hindsight. *Hageman* and *Salvati*

also fail to even recognize the advantages, benefits and/or properties of compositions having leucine and essential amino acids in accordance with the present claims. Instead, Applicant respectfully submits that the Patent Office is improperly using Applicant's patent application as a road map for creating hindsight obviousness. Accordingly, Applicant respectfully submits that the present claims are novel, nonobvious and distinguishable from the cited references and are in condition for allowance.

Accordingly, Applicant respectfully requests that the obviousness rejections be reconsidered and withdrawn.

For the foregoing reasons, Applicant respectfully requests reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims that could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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